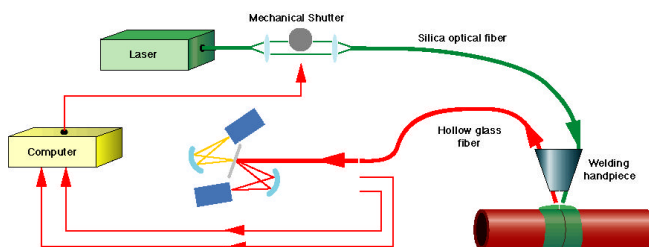


Laser Tissue Welding

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Researchers at the Lawrence Livermore National Laboratory are exploring new means of joining tissue without sutures. Laser tissue welding uses laser energy to activate photothermal bonds and/or photochemical bonds. Laser tissue welding can be used either without sutures or staples or as an adjunct technique to improve suture or staple strength or sealing characteristics. Tissue welding is a generic term that is also referred to as tissue fusion and vessel sealing. Besides lasers, which operate with wavelengths in the ultra violet, visible and infrared electromagnetic spectrum, other forms of energy (e.g. radio-frequency and microwave) are currently being used to join tissue. We use lasers because they provide the ability to accurately control the volume of tissue that is exposed to the activating energy.

Laser tissue welding can be augmented with solders. The solders serve two roles. First, the solders can include chromophores that are used to control the laser penetration such that it is concentrated at the fusion site. Since extrinsic chromophores are not limited to the absorption characteristics of native tissue or body fluids, solders may be tailored to selectively absorb energy that passes through normal tissue. Second, solders can include other biochemical constituents to improve the weld strength and/or weld leakage characteristics. Typical additives include native collagen, gelatinous collagen, fibrin, elastin and albumin. Also note that several investigators are using an extrinsic photochemical additive to help fuse tissue. The exact mechanism of tissue-tissue welding or welding with the extrinsic solders is a focus of current research in the field. A review of laser welding advances is presented in an article by Bass and Treat (Lasers in Surgery and Medicine, Vol. 17, pg. 315).

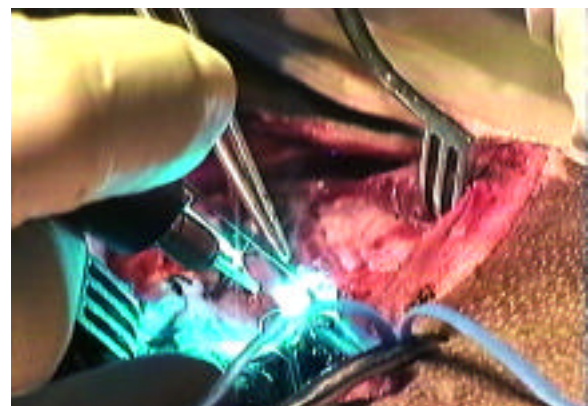


The architecture of our temperature feedback system. A two-color infrared temperature sensor is used to control the laser used to heat the weld site. The handpiece is directed at an end-to-end blood vessel anastomosis (joining), which is a typical application for our research. The blood vessel is coated with a solder to enhance laser absorption and acute repair strength. A patent is pending on the temperature sensor design.

In addition to solders, many researchers are also using feedback control to optimize and improve laser welding consistency. Temperature, scattering and birefringence are among the parameter candidates that are currently under investigation. Of these, temperature is the first parameter that has been developed into a feedback control system by the Medical Photonics Laboratory at LLNL.

Laser Tissue Welding Research at LLNL

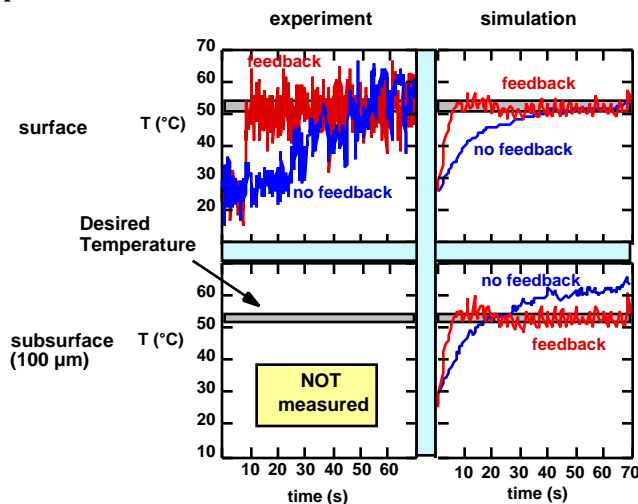
Laser tissue welding research centered at LLNL is a multi-team, multi-disciplinary effort that has three interdependent foci: (1) Diagnostic sensor development; (2) Energy deposition and sensor modeling; (3) Collagen crosslink biochemistry. LLNL is teamed with University of California at (UC) Davis biochemists and physicians at UC San Francisco and Harbor UCLA. We also have an active Cooperative Research and Development Agreement for laser tissue welding with an industrial partner, Conversion Energy Enterprises (CEE). Our efforts have resulted in three funding awards totaling \$1.6 million, 7 referred publications, and 2 patent applications.



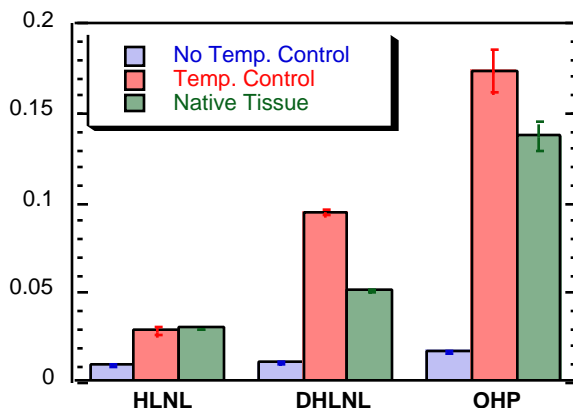
Photograph of our feasibility study performed at UCLA Harbor with Dr. Rodney White. The image shows the laser delivery handpiece with a hollow fiber for sensing temperature. The surgeon is repairing a 1 cm-long arteriotomy.

Our early work concluded with an *in vivo* feasibility test of our temperature sensor (Proc SPIE Vol. 2970, pg. 252, 1997; Lasers in Medical Science, accepted Sept. 1997). We documented substantially higher acute burst pressures using the temperature feedback to control welds compared with welds performed by an expert surgeon. Simulations of the experiment show that the open loop welds had higher, and potentially more damaging, internal temperatures (Journal of Biomedical Optics, Vol. 3 pg. 1, 1998). Our biochemistry

analysis of the weld sites showed that the improved strength might be due to an increase of strength-bearing collagen crosslinks in the feedback controlled welds relative to the uncontrolled welds (Proc SPIE Vol. 2970, pg. 261, 1997). In general, the early work allowed us to assemble the expertise and acquire the experience necessary to attack applied clinical problems.



Modeling results of the feasibility study. The simulations show that the open loop (no temperature feedback) welds result in significantly higher subsurface temperatures. The higher temperatures may cause excessive thermal damage. The simulations account for laser propagation, tissue absorption and scattering, water diffusion in the tissue, and evaporation at on the tissue surface.



Biochemistry results of the feasibility study. The covalent crosslinks labeled HLNL, DHLNL and OHP are bonds that have been previously linked to strength by Drs. J. Last and K. Reiser of UC Davis. Welds that used temperature feedback exhibited larger counts of the DHLNL and OHP crosslinks than the open loop or control (native tissue, no welding) samples.



Continued Research

Currently, we are engaged in laser welding research for the repair of congenital aorta defects in neonates. We are collaborating in this research with Drs. F. Hanley and A. Parry of UCSF, Drs. Last and Reiser of UC Davis and Dr. B. Soltz of CEE. The work is currently funded as part of a Department of Energy Center of Excellence in Laser Applications to Medicine and by a National Institutes of Health SBIR award. The preliminary results show that blood leakage can be reduced by 70% when laser welding is used as an adjunct to conventional sutures in artery repair.

We will continue to apply our expertise in lasers, multi-physics modeling, sensors, and instrumentation to laser tissue welding. We are currently involved in the development of birefringence and scattering sensors for controlling laser welding. With our UC Davis collaborators we will continue to research mechanisms of tissue welding and use that information to engineer welding techniques. Applications of interest include vessel repair and sealing, skin repair and minimally invasive surgery.

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